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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,489	06/23/2003	Ian David Manger	020174-008620US	1122

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/602,489	MANGER ET AL.	
	Examiner	Art Unit	
	PAUL S. HYUN	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 18-40* is/are pending in the application.

4a) Of the above claim(s) *1-13,32 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,15,18-31 and 34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 12, 2009 has been entered.

Claims 1-15 and 18-40 are currently pending wherein claims 38-40 are new and claims 1-13, 32 and 33 remain withdrawn pursuant to a restriction requirement. Applicant amended claims 14 and 34. In summary, claims 14, 15, 18-31 and 34-40 are pending for examination on the merits.

Despite the amendment, the rejections are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims **14, 15, 18-26, 28-31 and 34-40** are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. (US 2003/0008411 A1) in view of Quake et al. (US 2002/0037499 A1).

Van Dam et al. disclose a microfluidic device and a method for synthesizing a library of compounds by using the microfluidic device (see claim 15), which includes DNA synthesis (see [0056]). The device comprises a solid substrate layer and an elastomeric layer attached to the solid substrate wherein the surface of the solid substrate is immobilized with ligands for binding analytes of interest. The surfaces of both layers can comprise grooves/wells to define a plurality of first flow channels intersecting a plurality of second flow channels (see claim 24 and [0048]). The device further comprises a plurality of control channels associated with each of the flow channels. Upon the application of an actuation force within the control channels, the elastic surface of the control channels deflect into the flow channels and block fluid flow through the flow channels. The control channels also act as a pump for facilitating the movement of fluids through the flow channels (see [0068] and [0069]).

The method disclosed by the reference comprises the steps of:

- manipulating the control valves to restrict flow in the second flow channels,
- introducing a reagent into the first flow channels such that the reagent binds to the ligands immobilized to the surface of the solid substrate, and
- introducing a sample solution into the second flow channels such that the sample in the sample solution circulates through the flow channels and binds the reagents bound to the immobilized ligands (see claims 25 and 26).

The reference discloses that the term “reagent” refers to oligonucleotides, peptides, monomers, and other small molecules that are building blocks of a larger molecule (see [0056]). While the fluid is being introduced into one of the two flow

channels, the other set of flow channels is closed off by means of the control valves in order to prevent cross-contamination (see [0089]). The reference also discloses that reagents/samples that do not bind to the substrate are rinsed off using a solvent (see [0084]). The efficacy of the binding is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence (see [0122]). The method disclosed by Van Dam et al. differs from the claimed method in that Van Dam et al. do not disclose the step of manipulating the valves to form a closed loop.

Quake et al. disclose a microfluidic device similar to the device disclosed by Van Dam et al. Like the device disclosed by Van Dam et al., the device comprises intersecting microfluidic channels and elastomeric valves. Quake et al. also disclose a method for detecting analytes, the method comprising the steps of hybridizing a sample with probes immobilized to the surface of the microfluidic channels. Quake et al. also disclose the step of manipulating the valves to form a closed loop of flow channels. The closed loop enables the sample to circulate throughout the loop and properly hybridize with the probes (see Abstract and [0076]). Quake et al. also disclose the step of incubating the reaction to enable proper hybridization (see [0310]). In light of the disclosure of Quake et al., it would have been obvious to one of ordinary skill in the art to manipulate the valves of the Van Dam et al. device to form a closed loop of channels during the hybridization step to ensure that the sample and the reagents properly hybridize. It also would have been obvious to incubate the reaction to ensure proper hybridization.

With respect to claims 23-26, Van Dam et al. disclose the step of derivatizing the solid substrate and determining the efficacy of the derivatization (see [0122]). This is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence. In light of the disclosure, it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method described above and detect the fluorescence using a fluorescent microscope in order to observe the efficacy of the synthesis.

With respect to claim 31, given that the device disclosed by Van Dam et al. is adapted to perform binding assays, it would have been obvious to one of ordinary skill in the art to react any two entities that bind using the device disclosed by Van Dam et al., including a cell as the reagent and antimicrobes as the sample in order to observe the effects of the antimicrobes on the cell.

Claim **27** is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. in view of Quake et al. as applied to claims 14, 15, 18-26, 28-31 and 34-37, and further in view of Raillard et al. (US 2002/0102577 A1).

Van Dam et al. does not explicitly disclose the usage of a non-optical detector to observe the compound synthesis.

Raillard et al. disclose a method for labeling probes with radio-isotopes that emit radiation (see [0132]). The probe is detected using a detector that is sensitive to radiation.

In light of the disclosure of Raillard et al., it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method disclosed by Van Dam et al. with radio-isotope probes instead of fluorophores and detect the radiation using a radiation detector in order to observe the efficacy of the synthesis in the event that fluorophores are not available.

Response to Arguments

Applicant's arguments with respect to the claims have been fully considered but they are not persuasive.

First, Applicant argues that the structure of the claimed invention is patentably distinct from the microfluidic device disclosed by Van Dam et al. Specifically, Applicant argues that the device disclosed by Van Dam et al. does not comprise sets of loop forming control valves as recited in amended claims 14 and 34. This argument is not persuasive because intended use does not further limit the structure of the claimed invention. As indicated in the rejection, the device disclosed by Van Dam et al. comprises a valve at each channel inlet, outlet and channel intersection. These valves constitute sets of loop forming valves. It should be noted that the difference between the claimed invention and the disclosure of Van Dam et al. lies in the method of manipulating the valves. Structurally, the device disclosed by Van Dam et al. is not patentably distinct from the claimed invention.

Applicant also argues that Van Dam et al. do not disclose manipulating the valves as recited in the claims. Specifically, Applicant argues that Van Dam et al. do not disclose the step of manipulating the control valves to form closed loop channels. It

should be noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this instance, the motivation for manipulating the control valves disclosed by Van Dam et al. to form closed loop channels is provided by the disclosure of Quake et al. Quake et al. disclose a microfluidic device similar to the device disclosed by Van Dam et al. Like the device disclosed by Van Dam et al., the device comprises intersecting microfluidic channels and elastomeric valves. Quake et al. also disclose a method for detecting analytes, the method comprising the steps of hybridizing a sample with probes immobilized to the surface of the microfluidic channels. To facilitate hybridization, Quake et al. disclose the step of manipulating the valves to form a closed loop of flow channels. The closed loop enables the sample to circulate and properly hybridize with the probes (see Abstract and [0076]). The Examiner maintains the position that Quake et al. provide sufficient motivation to manipulate the control channels disclosed by Van Dam et al. to form a plurality of closed loop flow channels.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL S. HYUN whose telephone number is (571)272-8559. The examiner can normally be reached on Monday-Friday 8AM-4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Paul S Hyun/
Examiner, Art Unit 1797

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797